Applicant hereby represents that the changes introduced into the specification and claims by the present Amendment do not add new matter to the application.

Rejection of claims 1-2, 5-6, 9-10, 13-14, 18-19, and 22-23 under 35 U.S.C. 112, first paragraph

Claims 1-2, 5-6, 9-10, 13-14, 18-19, and 22-23 were rejected under 35 U.S.C. 112, first paragraph. The Examiner has argued that the present specification does not reasonably provide enablement for [1] all methods of screening all chemicals; [2] the use of all assay formats; [3] use of all assay systems as part of the claimed screening method, wherein such assay system included the use of all chemical or biological reaction compounds for the detection of a desired chemical or biological reaction. However, the Examiner has conceded that the claims are enabling for "screening strategies associated with the following different classes of chemical compounds as affecting aspects of the cell cycle, as indicated by these examples from the instant specification:" citing Examples 6, 7, 9, 10 and 11.

Applicant strongly disagrees that claims 1-2, 5-6, 9-10, 13-14, 18-19, and 22-23 are not enabled. However, in order to advance prosecution of the application, Applicant has cancelled claims 1-2, 5-6, 9-10, 13-14, 18-19, and 22-23 by amendment rendering the rejection moot. In addition, Applicant has added new claims 41-56. Applicant submits that the present specification fully provides enablement to the new claims 41-56.

The present specification teaches the use of a plurality of reaction vessels having volumes of liquid ranging from 200 microliters to approximately 250 nanoliters. Support for the stated volumes is found in the claims as filed (claims 14-17). More specifically, the specification teaches the use of standard 96 well plates, 384 well plates where the plates have similar dimensions (width, length and thickness) as the 96 well plates but having smaller reaction vessel volumes (Figure 2), 1536 well plates where the plates have similar dimensions as the 96 well plates but having even smaller reaction vessel volumes (Figure 3), and 6144 well plates where

the plates have similar dimensions as the 96 well plates but having smaller reaction vessel volumes (Figure 4).

It is readily appreciated by those of ordinary skill in the art, which is high in the area of biotechnology (i.e. Ph.D. level researcher), that the present invention is a method of screening compounds and can be used to screen any library of test compounds. While the examples in the specification teach the use of several classes of compounds in the present invention, the scope of the invention is not limited to screening only those compounds described in the Examples (MPEP 2164.08a). It is clear that the present specification teaches those skilled in the art how to screen any test compound(s) using the presently claimed invention. General descriptions and references of libraries of natural compounds and synthetic compounds are found in the specification on pages 39-40. Furthermore given the high level of knowledge and high skill in the art, those skilled in the art readily appreciate that any library of test compounds available to them can be screened using the presently claimed invention. As such, there is no undue experimentation in providing libraries of test compounds for screening because any compound can be tested and any library of test compounds can be screened. Therefore, the present specification fully enables the screening of any library of test compounds without undue experimentation.

The rejection by the Examiner that the present specification does not reasonably provide enablement for the use of all assay formats and for the use of all assay systems as part of the claimed screening method is rendered moot by the cancellation of claims 1-2, 5-6, 9-10, 13-14, 18-19, and 22-23.

Rejection of claims 1-2, 5, 9-10, 13-14, 18, and 22-23 under 35 U.S.C. 112, second paragraph

The Examiner has rejected claims 1-2, 5-6, 9-10, 13-14, 18-19, and 22-23 for indefiniteness. Cancellation of these claims renders the rejection moot. Furthermore, the newly added claims do not include the language said to be indefinite.

Rejection of claims 1-2, 5-6, 9-10, 13-14, 18-19, and 22-23 under 35 U.S.C. 103 over:

1) Gallop et al. (USP 5,525,734; "Gallop"), Manns (USP 4,948,442; "Manns"), page 29, lines 6-19 of the present application, and Craig ("Chapter 14, Screening Combinatorial Libraries," A Practical Guide to Combinatorial Chemistry, Czarnik and DeWitt eds., Washington D.C.: American Chemical Society, 1997; "Craig");

2) Zambias et al. (USP 5,736,412; "Zambias"), Manns, page 29, lines 6-19 of the present application, and Craig; and

3) Godowski et al. (USP 6,025,145; "Godowski"), Manns, page 29, lines 6-19 of the present application, and Craig.

Claims 1-2, 5-6, 9-10, 13-14, 18-19, and 22-23 have been canceled and replaced with claims 41-56 rendering the rejection under 35 U.S.C. §103 moot. New claims 41-56 have been added. To provide a clear record, Applicant respectfully disagrees with the Examiner's reasons for rejection as applied to new claims 41-56, and traverses the Examiner's rejection. Applicant submits that claims 41-56 are not obvious over 1) Gallop, Manns, page 29 lines 6-19 of the present application and Craig; 2) Zambias, Manns, page 29 lines 6-19 of the present application and Craig; and 3) Godowski, Manns, page 29 lines 6-19 of the present application and Craig.

Gallop teaches methods of synthesizing and screening pyrrolidine compound libraries on solid supports. The Examiner states in the Official Action that Gallop also teaches screening the library for biological or pharmaceutical activity. However, the Examiner has conceded that Gallop does not suggest or teach a method of screening compounds where the volume of each reaction vessel is less than or equal to approximately 200 microliters.

Zambias teaches a method of synthesizing an (m x n) array of different chemical compounds wherein each of the compounds has at least one structural diversity element selected from a group of amines and ketones and wherein the scaffold structure is selected from a group consisting of aminimide, imidazolone, sulfonylaminimide and phosphonylaminimide (see abstract of Zambias). As stated by the Examiner in the Official Action, Zambias teaches simultaneous screens for assaying large numbers of parallel compound samples for exploring

biological activity. However, the Examiner has conceded that Zambias does not suggest or teach a method of screening compounds where the volume of each reaction vessel is less than or equal to approximately 200 microliters.

Godowski teaches an assay for measuring activation of a tyrosine kinase receptor. The method of Godowski involves contacting cells with a ligand to assay the ability of the ligand to affect activation of the auto-phosphorylation. After the cells are exposed to the ligand, the cells are lysed. The lysate is removed and transferred to a second solid phase containing a capture agent. The second solid phase is washed to remove unbound cell lysate. The captured tyrosine kinase receptor is then contacted with anti-phosphotyrosine antibodies and the levels of the antibodies are measured. However, the Examiner has conceded that Godowski does not suggest or teach a method of screening compounds where the volume of each reaction vessel is less than or equal to approximately 200 microliters. Furthermore, Applicant submit that Godowski does not teach introducing a ligand (i.e. capture agent) that binds specifically to a biological component into each reaction vessel.

Manns teaches a standard 96 well micro-titre test plate and methods for producing the plates where the plates contain an incubation tray, a filter and a harvester tray having mating ridges and grooves to prevent cross-talk between the wells along the filter (see Abstract). Craig teaches methods of producing large numbers of compounds for testing against a number of biological targets.

Applicants submit that new claims 41-56 are not obvious over the combinations of cited references because the combinations of the references cited do not teach all of the claim limitations. The Examiner has conceded that the references differ from the claimed invention in that they do not teach the screening of compounds in a plurality of reaction vessels where the volume of each reaction vessel is less than or equal to approximately 200 microliters. In addition with regard to Claim 41 and its dependent claims, there is no suggestion or teaching in the references to use a ligand that binds specifically to a biological component which is an intracellular product to study a biological process. Furthermore, with regard to Claim 42 and its

dependent claims, there is no suggestion or teaching in the references that each reaction vessel has a volume of liquid less than or equal to approximately 50 microliters. Therefore, new claims 41-56 are not obvious over the combination of cited references.

Moreover, Applicant submits that the Examiner has applied an improper "obvious to try" rationale in support of the rejection of the examined claims as obvious under 35 U.S.C. §103. While it may have been "obvious to try" to combine the teachings of Gallop, Manns and Craig; Zambias, Manns and Craig; and/or Godowski, Manns and Craig, there was no reasonable expectation of success in the combinations in order to achieve the claimed invention. Claim 41 and its dependent claims state, as an element in the step of introducing a ligand into each reaction vessel, that a ligand is used to bind specifically to a biological component which is an intracellular product of a biological process. There is no reasonable expectation of success that an intracellular product of a biological process can be detected by binding specifically to a ligand in volumes less than or equal to approximately 250 microliters.

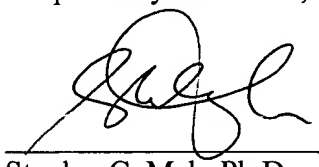
In addition, Claim 42 and its dependent claims state, as an element in the step of providing a plurality of reactions vessels, that each reaction vessel has a volume less than or equal to approximately 50 microliters. Although it may be obvious to try, there is no reasonable expectation of success that a product of a biological process can be detected at such small volumes (less than 50 microliters). However, the present invention as described in the specification in the Examples, demonstrated experimentally that ligands can be used to bind specifically to an intracellular product of a biological product in volumes as small as 250 nanoliters to detect activity of a biological process.

Since there is no reasonable expectation of success in combining the teachings of Gallop, Manns and Craig to achieve the claimed invention and since the references do not teach all of the claim limitations, claims 41-56 are not obvious over Gallop in view of Manns and in view of Craig.

Applicants submit that the claims as amended are now in condition for allowance. Early favorable action is requested.

Please charge any fees that may be required, or credit any overpayment, to our Deposit Account No. 03-1721.

Respectfully submitted,



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